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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/099,307 06/18/98 ERTL

J 02481.1597

HM22/0228

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EXAMINER

SAGUD, C.

ART UNIT

PAPER NUMBER

1646

DATE MAILED:

02/28/00

13

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Office Action Summary

Application No.  
**09/099,307**

Applicant(s)  
**ERTL et al.**

Examiner  
**Christine Saoud**

Group Art Unit  
**1646**



☒ Responsive to communication(s) filed on Dec 2, 1999

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

## Disposition of Claims

☒ Claim(s) 1-36, 41-58, and 61-67 is/are pending in the application.

Of the above, claim(s) 2-27, 29-36, 41-58, and 61-67 is/are withdrawn from consideration.

☐ Claim(s) \_\_\_\_\_ is/are allowed.

☒ Claim(s) 1 and 28 is/are rejected.

☐ Claim(s) \_\_\_\_\_ is/are objected to.

☐ Claims \_\_\_\_\_ are subject to restriction or election requirement.

## Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

☒ The proposed drawing correction, filed on Dec 2, 1999 is ☒ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some\* ☐ None of the CERTIFIED copies of the priority documents have been  
☐ received.

☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Art Unit: 1646

## **DETAILED ACTION**

### ***Response to Amendment***

1. Claims 1-36, 41-58, and 60-67 are pending in the instant application. Claims 2-27, 29-36, 41-58 and 60-67 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected species, the requirement having been traversed in Paper No. 8.

Claims 1 and 28 are currently under examination.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

4. Applicant's arguments filed 02 December 1999 have been fully considered but they are not deemed to be persuasive.

### ***Sequence Compliance***

5. The CRF which was submitted with paper #12 has been entered.

Art Unit: 1646

*Drawings*

6. The corrected or substitute drawings were received on 02 December 1999. These drawings are acceptable.

*Claim Rejections - 35 USC § 103*

7. Claims 1 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brange (U.S. Pat. No. 5,597,796) in view of Markussen et al. (WO 92/00321) and Brange et al. (WO 89/10937) for the reasons of record in paper #9.

Applicant argues that Brange ('796) does teach substitution of positions B3 and B29, but does not teach substitution of B3 with any other residue except one having a negative charge at neutral pH. Applicant is correct that Brange ('796) does teach substitution of B3 with Asp or Glu. The rejection should have been more specific in that Brange ('796) does not teach substitution of B3 with a basic amino acid.

Applicant argues that Brange ('796) teaches away from the claimed invention because substitutions at B3 are taught, but that substitution with a basic amino acid is not suggested, therefore, teaching away from this substitution. This argument is not persuasive because Brange ('796) does not require the substitution of B3 to arrive at the result of reduced tendency to association. The substitution of B3 is taught, but not required for the desired activity whereas the substitution B29 is specifically suggested at column 8, lines 17-19.

Art Unit: 1646

Applicant argues that because Brange ('796) teaches that insulin analogs with a greater negative charge are desirable for reduced tendency to association, then there is no motivation to combine a modification of B3 to a positive charge. However, Markussen et al. teach substitution of any one of amino acids B1 to B6 with a basic amino acid residue; i.e. a lysine (Lys) or arginine (Arg) in order to prolong insulin action. The teaching of Brange ('796) is that a more negatively charged insulin is less likely to aggregate, therefore, one would be motivated to include a substitution of Brange ('796) with the substitution of Markussen et al. because the Markussen modification would increase the potential for aggregation which would be compensated by the modification of Brange ('796). One would be motivated to combine the modifications in order to receive the combined benefit as taught by Brange et al. Therefore, it would have been *prima facie* obvious at the time of the instant invention to make the insulin analogue of Brange wherein the amino acid at position B29 is substituted with Glu and combine the substitution of Lys for B3 as taught by Markussen et al. in order to obtain an insulin analogue which is stabilized against association and also has a prolonged insulin action, absent evidence to the contrary.

### ***Conclusion***

8. No claim is allowed.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO**

Art Unit: 1646

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine Saoud, Ph.D., whose telephone number is (703) 305-7519. The examiner can normally be reached on Monday to Friday from 8AM to 3PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for this Group is (703) 308-0294.

Official papers filed by fax should be directed to (703) 308-4227. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Christine Saoud, Ph.D.  
February 24, 2000



JOHN ULM  
PRIMARY EXAMINER  
GROUP 1800